

1 We claim:

1 1. A method to isolate *d-threo*-methylphenidate in greater than 99 percent
2 enantiomeric excess from a mixture of *d-threo*-methylphenidate and *l-threo*-methylphenidate,
3 comprising the steps of:
4 providing a mixture comprising *d-threo*-methylphenidate and *l-threo*-methylphenidate;
5 supplying *l*-fenchyloxyacetic acid;
6 treating said mixture with said *l*-fenchyloxyacetic acid;
7 collecting *d-threo*-methylphenidate having greater than a 99 percent enantiomeric excess.

1 2. The method of claim 1, wherein said supplying step further comprises the steps
2 of:
3 providing *l*-fenchyl alcohol;
4 providing chloroacetic acid;
5 reacting said *l*-fenchyl alcohol with said chloroacetic acid to form said *l*-fenchyloxyacetic
6 acid.

1 3. The method of claim 1, wherein said treating step includes the following steps:
2 reacting said mixture with said *l*-fenchyloxyacetic acid;
3 isolating the salt of (1R)-endo-(+)-fenchyloxyacetic acid and *d-threo*-methylphenidate;
4 and
5 cracking said salt of (1R)-endo-(+)-fenchyloxyacetic acid and *d-threo*-methylphenidate.

1 4. The method of claim 3, wherein said cracking step includes the following steps:
2 providing a 10 percent solution of sodium bicarbonate in water;

3 treating the salt of (1R)-endo-(+)-fenchyloxyacetic acid and *d-threo*-methylphenidate
4 with said aqueous sodium bicarbonate solution and ethyl acetate to give a two phase mixture
5 comprising a water fraction and an ethyl acetate fraction;
6 separating the ethyl acetate fraction from said water fraction; and
7 treating said ethyl acetate fraction with hydrochloric acid.

1 5. The method of claim 4, further comprising the steps of:
2 obtaining *l-threo*-methylphenidate from said water fraction;
3 hydrolyzing said *l-threo*-methylphenidate to 1-ritalinic acid;
4 reacting said 1-ritalinic acid with a methanol solution saturated with hydrogen chloride to
5 form *dl*-methylphenidate.

1 6. A method to isolate *d-threo*-methylphenidate in greater than 99 percent
2 enantiomeric excess from a racemic mixture of *d-threo*-methylphenidate and *l-threo*-
3 methylphenidate, comprising the steps of:
4 providing a racemic mixture comprising *d-threo*-methylphenidate and *l-threo*-
5 methylphenidate;
6 obtaining a second mixture of *d-threo*-methylphenidate and *l-threo*-methylphenidate from
7 said racemic mixture, wherein said second mixture comprises *d-threo*-methylphenidate having
8 greater than a 90 percent enantiomeric excess;
9 supplying *l*-fenchyloxyacetic acid;
10 treating said second mixture with said *l*-fenchyloxyacetic acid;
11 collecting *d-threo*-methylphenidate having greater than a 99 percent enantiomeric excess.

1 7. The method of claim 6, wherein said obtaining step includes passing said racemic
2 mixture through a chiral column chromatograph.

1 8. The method of claim 6, wherein said obtaining step includes the steps of:
2 reacting said racemic mixture with an optically active acid in methanol to give insoluble
3 solids and a methanolic solution;
4 separating said insoluble solids and said methanolic solution;
5 adding water to said methanolic solution;
6 filtering said water / methanol solution to collect said second mixture.

1 9. The method of claim 8, wherein said treating step includes:
2 reacting said second mixture with said *l*-fenchyloxyacetic acid;
3 isolating the salt of (1R)-endo-(+)-fenchyloxyacetic acid and *d*-threo-methylphenidate;
4 and
5 cracking said salt of (1R)-endo-(+)-fenchyloxyacetic acid and *d*-threo-methylphenidate.

1 10. The method of claim 9, wherein said cracking step includes the following steps:
2 providing a 10 percent solution of sodium bicarbonate in water;
3 treating the salt of (1R)-endo-(+)-fenchyloxyacetic acid and *d*-threo-methylphenidate
4 with said aqueous sodium bicarbonate solution and ethyl acetate to give a two phase mixture
5 comprising a water fraction and an ethyl acetate fraction;
6 separating the ethyl acetate fraction from said water fraction; and
7 treating said ethyl acetate fraction with hydrochloric acid.

1 11. The method of claim 8, wherein said insoluble solids comprises the adduct of *l*-
2 threo-methylphenidate and said optically active-acid, further comprising the steps of:
3 forming 1-ritalinic acid from said insoluble solids;
4 providing a saturated solution of hydrogen chloride in methanol;
5 esterifying said 1-ritalinic acid using said saturated solution to form said racemic mixture.

6 12. A method to resolve stereoisomers of an optically active compound comprising an
7 amine moiety, comprising the steps of:
8 providing a mixture comprising two stereoisomers of a compound comprising a amine
9 moiety;
10 supplying *l*-fenchyloxyacetic acid;
11 treating said mixture with said *l*-fenchyloxyacetic acid;
12 collecting one of said two or more stereoisomers having greater than a 99 percent
13 enantiomeric excess.